

CLAIMS

- 1 1. A crystallization parameter optimization process comprising the
2 steps of:
3 selecting a plurality of physical characterization input variables to
4 define a total crystallization experiment permutation number for a crystallant;
5 performing a plurality of crystallization experimental samples, said
6 plurality of crystallization experimental samples being less than the total
7 crystallization experiment permutation number;
8 training a predictive crystallization function through analysis of said
9 plurality of crystallization experimental samples; and
10 determining an optimal physical crystallization parameter from said
11 predictive crystallization function.
- 1 2. The process of claim 1 wherein said predictive crystallization
2 function is a neural network.
- 1 3. The process of claim 1 wherein said crystallant is a protein.
- 1 4. The process of claim 1 wherein each of said plurality of physical
2 crystallization input variables is selected from a group consisting of:
3 temperature, protein dilution, anionic precipitate, organic precipitate, buffer
4 pH, precipitation strength, organic moment, percent glycerol, additive, divalent
5 ion, gravity, light, magnetism, atmosphere identity, and atmosphere pressure.

1 5. The process of claim 1 wherein the plurality of crystallization
2 experimental samples performed is less than 5% of the total crystallization
3 experiment permutation number.

1 6. The process of claim 1 wherein the plurality of crystallization
2 experimental samples performed is less than 0.1% of the total crystallization
3 experiment permutation number.

1 7. The process of claim 1 wherein said predictive crystallization
2 function analyzes a crystallization experimental sample as to a status selected
3 from the group consisting of: clear drop, phase change, precipitate, and
4 spherulettes.

1 8. The process of claim 1 wherein said predictive crystallization
2 function trains through back propagation.

1 9. The process of claim 8 wherein said predictive crystallization
2 function includes a hidden layer intermediate between input values and said
3 optimal physical crystallization parameter.

1 10. The process of claim 1 wherein the performance of said
2 plurality of crystallization experimental samples is automated.

1 11. The process of claim 10 further comprising the step of
2 communicating said plurality of physical crystallization input variables
3 between a manufacturing execution system performing said plurality of
4 experimental samples and said predictive crystallization function.

1 12. The process of claim 1 further comprising the step of
2 communicating said predictive crystallization function to a database.

1 13. The process of claim 12 wherein said database includes
2 characteristics of a crystallization sample.

1 14. The process of claim 1 further comprising the steps of
2 attempting crystal growth using said optimal physical crystallization parameter.

1 15. The process of claim 14 further comprising the step of
2 communicating on said crystal growth attempt to a shared database.

1 16. The process of claim 15 further comprising the step of
2 classifying said crystal growth attempt on a basis selected from the group
3 consisting of: said optimal physical crystallization parameter, said predictive
4 crystallization function, and a physical property of a crystallant.

1 17. The process of claim 1 wherein performing said plurality of
2 crystallization experimental samples comprises the steps of:
3 controlling a plurality of variables where each of said plurality of
4 variables assumes an index value or plurality of index values; and
5 performing a Chernov analysis to derive a minimized combined
6 quantity representative of said total crystallization permutation number.

1 18. The process of claim 1 wherein said plurality of crystallization
2 experimental samples are converted to vectors prior to the training of said
3 predictive crystallization function.

1 19. The process of claim 18 further comprising the step of
2 clustering said vectors.

1 20. The process of claim 19 wherein clustering occurs through the
2 application of an analysis selected from the group consisting of: a neural net, a
3 Chernov algorithm, a Bayesian net, a Bayesian classification schema, and a
4 Bayesian decomposition.

1 21. A crystallization parameter optimization process comprising the
2 steps of:

3 selecting a plurality of physical characterization input variables for a
4 known crystallant to define a total crystallization experiment permutation
5 number;
6 performing a plurality of crystallization experimental samples on said
7 known crystallant;
8 training a predictive crystallization function through analysis of said
9 plurality of crystallization experimental samples;
10 determining an optimal physical crystallization parameter for said
11 known crystallant;
12 storing said optimal physical crystallization parameters and a physical
13 property of said known crystallant sample in a classification system; and
14 comparing an unknown crystallization sample to the classification of
15 said known crystallant.

1 22. The process of claim 21 wherein said predictive crystallization
2 function is a neural network.

1 23. The process of claim 21 wherein said classification system is
2 based on an aspect selected from the group consisting of: nodal basis functions,
3 nodal construction similarities, and contribution of a particular physical
4 characterization input variable.

1 24. The process of claim 21 wherein a comparative neural network
2 relates said known crystallant and said unknown crystallization sample.

1 25. The process of claim 21 wherein said classification system is
2 self-learning.

1 26. The process of claim 21 wherein said classification system is
2 self-organized.

1 27. The process of claim 21 wherein each of said plurality of
2 physical crystallization input variables is selected from a group consisting of:
3 temperature, protein dilution, anionic precipitate, organic precipitate, buffer
4 pH, precipitation strength, organic moment, percent glycerol, additive, divalent
5 ion, gravity, light, magnetism, atmosphere identity, and atmosphere pressure.

1 28. The process of claim 21 wherein the performance of said
2 plurality of crystallization experiments is automated.

1 29. The process of claim 21 further comprising the steps of
2 attempting crystal growth using said optimal physical crystallization parameter.

1 30. The process of claim 21 wherein performing said plurality of
2 crystallization experimental samples comprises the steps of:

3 controlling a plurality of variables where each of said plurality of
4 variables assumes an index value or plurality of index values; and
5 performing a Chernov analysis to derive a minimized combined
6 quantity representative of said total crystallization permutation number.

1 31. The process of claim 21 wherein storage occurs in a shared
2 database wherein said shared database also stores at least one type of protein
3 information selected from the group consisting of: protein expression gene;
4 protein characteristics; protein class hierarchy; actual protein chemical
5 structure including primary, secondary, tertiary and where applicable
6 quaternary structures; protein crystal generation recipe parameters; and optimal
7 crystallization screen design.

1 32. A protein crystal derived by the process of claim 1.

1 33. A neural network having been trained through analysis of a
2 plurality of crystallization experimental samples to predict optimal
3 crystallization conditions for a protein.

1 34. The network of claim 33 wherein said plurality of samples
2 comprises samples failing to yield crystals.

1 35. A system for crystallization parameter optimization, the system
2 comprising:
3 a database having a plurality of input variables, each of said plurality of
4 input variables having a value range;
5 an incomplete factorial screen program having a trainable predictive
6 crystallization function;
7 a computer capable of executing the incomplete factorial screen
8 program to determine an optimal crystallization parameter; and
9 a manufacturing execution system for automatically acquiring of a
10 datum from each of a plurality of crystallization experimental samples,
11 analyzing and archiving of data from the incomplete factorial screen program.

1 36. The system of claim 35 wherein said manufacturing execution
2 system controls at least one piece of crystallization hardware selected from the
3 group consisting of: a liquid dispenser, a crystallant dispenser, a robotic
4 handler, an imaging system, a sample centering motor relative to a camera
5 focal plane, and a lighting system.

1 37. The system of claim 36 wherein said sample centering motor is
2 coupled to at least one of: a sample stage and said camera for automatically
3 positioning the specimen within the focal plane of said camera.

1 38. The system of claim 35 further comprising a barcode for
2 indexing each of said plurality of samples.

1 39. The system of claim 36 further comprising a centering algorithm
2 coupled to said motor for converging a central region of the specimen with a
3 central region of the camera focal plane.

1 40. The system of claim 39 wherein said centering algorithm
2 operates automatically.

1 41. The system of claim 35 further comprising a drop identification
2 algorithm for evaluating a liquid drop associated with each of said plurality of
3 samples.

1 42. The system of claim 41 wherein the liquid drop is classified into
2 a preselected plurality of classes.

1 43. The system of claim 42 wherein said drop identification
2 algorithm operates automatically.

1 44. The system of claim 36 wherein said motor is coupled to said
2 camera.

1 45. The system of claim 36 further comprising scheduling software
2 interfaced with said robotic handler.

1 46. The system of claim 37 wherein said scheduling software is
2 interfaced with said sample stage.

1 47. The system of claim 35 further comprising a database that stores
2 crystal relevant parameters.

1 48. The system of claim 47 wherein said crystal relevant parameters
2 include at least one parameter of the group consisting of: crystal weight,
3 crystal specimen pH, crystal specimen temperature, crystal specimen protein
4 type, detergents present, additives present, preservatives present, reservoir
5 buffer present, reservoir buffer concentration, reservoir buffer pH, crystal
6 specimen volume, notes, crystal specimen score, and crystal specimen drop
7 descriptor.

1 49. The system of claim 47 wherein said database is relational
2 between said predictive crystallization function and said crystal parameters.

1 50. The system of claim 47 wherein said database is connected to a
2 structured query language database.

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1 51. A protein crystal derived from a system of claim 35.

1 52. A process according to claim 1 substantially as described herein
2 in any of the examples.